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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,128	11/27/2001	Alan N. Houghton	MSK.P-026-3	3698

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,128	HOUGHTON ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *7-9, 14-16, 18, 25-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10-13,17,19-24,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/07/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Election/Restrictions

1. Upon reconsideration the Group II (claims 1, 3, 4, 6, 10, 11, 13, 19, 20, 23 and 24, to the extent the claims read on human gp75) will be examined with the elected Group I.

2. Claims 1-29 are pending.

Claims 28 and 29 have been added.

Claims 3, 7-9, 14-16 and 25-27, drawn to non-elected inventions are withdrawn from examination.

Claims 1-6, 10-13, 17-24, 28 and 29 are examined on the merits to the extent that the xenogeneic differentiation antigen is a human tyrosinase and human gp75.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

4. Claims 28 and 29 are objected to because of the following informality: they both reference non-elected subject matter, i.e. Melan-A/Mart-1. Correction is required.

New Grounds of Rejection and Maintained Grounds of Rejection

Claim Rejections - 35 USC § 112

5. The rejection of claims 1-6, 10, 11, 19, 20, 21, 23, 28 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating canine melanoma comprising the step of administering to an immunologically-effective amount of a xenogeneic differentiation antigens, human tyrosinase and human gp75, does not reasonably provide enablement for the broad treatment of melanoma in a mammalian subject comprising the step of administering the broad class of xenogeneic differentiation antigens is maintained and made. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants aver "...Eck...relates to a broad range of 'therapeutic gene therapy'" and the types of problems noted by the Examiner are associated with the broad concept of therapy and are of no apparent relevance to the claimed invention, see Remarks submitted August 7, 2005. Applicants argue that the specification yields two examples of two species with two different melanoma differentiation antigens and a person skilled in the art would not question the broader applicability of the claimed invention. These arguments and points of view have been carefully considered but found unpersuasive.

Eck does provide reason to doubt the implementation of a broad category xenogeneic differentiation antigens in the treatment of melanoma. And while Applicants have considered the reference not valid of doubting the claimed invention the art provides for such. The art of gene therapy in an unpredictable art with respect with cell

targeting, levels of expression of a therapeutic protein necessary to provide therapy and the mode of administration of the therapeutic gene. These issues are discussed by two published reviews. Verma *et al.* teach that as of 1997, "there is still no single outcome that we can point to as a success story" (page 239, col. 1). The authors go on to state, "Thus far, the problem has been an inability to deliver genes efficiently and to obtain sustained expression" (page 239, col. 3). Anderson (1998) states that "there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of a human disease" (page 25, col 1) and concludes, "Several major deficiencies still exist including poor delivery system, both viral and no-viral, and poor gene expression after genes are delivered" (page 30). Besides the general expectation that it will require years of further research to develop effective gene therapy (Anderson, page 30), it would require extensive research to understand the fundamental biology of the system. Moreover, Applicant's claims do recite any particular mode of administration of a therapeutic gene or a means to target tissue with a therapeutic gene. The specification however, has not provided any specific guidance or teachings with regard to the other modes of cell targeting or modes of administering a therapeutic gene encompassed by the claims. While progress has been made in recent years for gene transfer *in vivo*, vector targeting to desired tissues *in vivo* continues to be unpredictable and inefficient as supported by numerous teachings available in the art. For example, Miller (1995, FASEB J., Vol. 9, pages 190-199) review the types of vectors available for *in vivo* gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting

strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art, which shows promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal (1995, Science, Vol. 270, page 404-410) also reviews various vectors known in the art and indicates that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409). It should be noted that although the publication date of these cited references is prior to the filing date of the instant application, the issues regarding the unpredictability of gene therapy remain the same and have not be resolved by the guidance provided by the instant specification.

The specification provides guidance as to how to target the administered human

tyrosinase nucleic acids to the non-human dog subjects and human gp75 to non-human subjects. However, the instant specification does not teach how to overcome problems with *in vivo* delivery and expression with respect to the broad genus of differentiation antigen as claimed. The state of the art regarding in vivo delivery of nucleic acids is highly unpredictable.

Given the lack of guidance from the specification one of ordinary skill in the art would be subject to undue experimentation without reasonable expectation of success to practice the broadly state method of treatment. Therefore, in view of the quantity of experimentation necessary to determine the parameters listed above for the treatment of a disease, particularly melanoma, the unpredictable state of the art with respect to gene therapy, and the breadth of the claims it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1, 4, 10 and 11 rejected under 35 U.S.C. 102(a) as being anticipated by Zhai et al. (The Journal of Immunology 156: 700-710, January 1996). Zhai discloses a method of inducing specific T cell immunity for melanoma treatment. Xenogenic differentiation antigens, human MART-1 and gp100 expressed in recombinant

adenoviruses were administered to C57BL/6 mice and rendered a protective affect against murine melanoma.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-6, 10-13 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhai et al. (The Journal of Immunology 156: 700-710, January 1996), and further in view of U.S. Patent number 5,773,291 (filed January 23, 1995/ IDS reference, submitted May 23, 2003). The teachings of Zhai have been presented in the 102(a) rejection.

Zhai does not teach a method for treating melanoma in a mammalian subject comprising administration of a human tyrosinase xenogeneic differentiation antigen or a human gp75 of the same type as the differentiation antigen expressed by melanoma cells of the said subject. However, the patent teaches the expression of biologically active human tyrosinase, a tumor-associated antigen (TAA).

It would have been *prima facie* obvious at the time of the claimed invention was made to use tyrosinase or gp75 as a xenogeneic differentiation antigen to be administered in the melanoma treatment exemplified by Zhai. One of ordinary skill in

the art would have been motivated to do so with a reasonable expectation of success because it is well known in the art that tyrosine quite like MART1 and gp100 are recognized as TAAs implicated in the development of cancer vaccines, see Zhai, page 700, column 1. Moreover, one of ordinary skill in the art would have been motivated to substitute gp100 and MART1 with human tyrosinase or human gp75 in order to establish another successful mode of melanoma treatment.

Double Patenting

9. The provisional rejection of claims 1, 2, 4, 5, 10-12, 17 and 19-24 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-19 of copending Application No. 10/041,410 (filed January 7, 2002) is maintained. Claims 1-6, 8 and 11-13 of the copending application have been cancelled.

Applicants noted that an action on the merits had yet to be received. At this point in prosecution a First Action on the Merits has been mailed. And the instant rejection is still valid. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
31 October 2005